

## Uterine myoma with massive lymphocytic infiltration – case report

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### Abstract

**Introduction:** Uterine leiomyomas are the most common neoplasm of the uterus in women. Massive lymphocytic infiltration in a myoma is an unusual finding. It is characterised by the varying intensity of lymphocyte infiltration, the presence of scattered plasma cells, eosinophilia, and rarely, other items. We would like to call attention to such a rare lesion.

**Case description:** We present the case of a 31-year-old woman who had undergone surgical excision of a uterine tumour. Grossly, it had the typical uterine smooth muscle wall consistency. The microscopic examination revealed leiomyoma with heavy infiltration composed mainly of lymphocytes. On immunohistochemistry, in the lymphocytic infiltrate the T mature (CD3+/CD5+/TdT-) lymphocytes, small and of cytotoxic (CD8+/CD56-) type, prevailed, with moderate proliferative activity (expression of Ki67 found in ca. 30-40% of the cells), whereas B lymphocytes (CD20+/CD5-/TdT-) were innumerable and present in nodular aggregates. Despite a strong suspicion of neoplastic lymphoproliferation, the histopathological diagnosis was: leiomyoma with massive lymphoid infiltration. The cause of this feature is not known, although the gonadotropin-releasing hormone agonist and post-menopausal processes may promote such transformations. In differential diagnosis, malignant lymphoma, inflammatory pseudotumour, and pyomyoma should be included.

**Conclusions:** Lymphocytic infiltration within the uterine myoma is rare. The recognition of its distinct histological features is important to avoid possible misdiagnosis.

**Key words:** myoma, leiomyoma, lymphoma, neoplasms, gonadotropins, menopause.

### Introduction

Uterine leiomyomas (called popularly fibroids) are benign tumours, and they are an important factor lowering the quality of life. Uterine leiomyoma with massive lymphocyte infiltration is a rare and unusual pathological finding. Twenty such cases have been described in the available literature [1]. They are characterised by varying intensity of lymphocyte infiltration, the presence of scattered plasma cells, eosinophilia, and rarely, other items [2]. A case of this atypical lesion is reported in a 31-year-old woman who had undergone surgery for a uterine tumour. Macroscopically, it did not differ from typical fibroids. Microscopic examination revealed a leiomyoma diffusely infiltrated by lymphocytes, with a suspicion of neoplastic lymphoproliferation.

### Case report

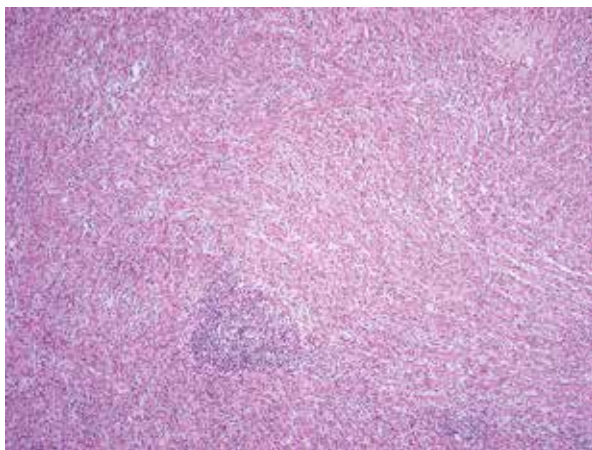
Written, informed consent was obtained from the patient for her data to be used for publication. A 31-year-old woman, nulliparous, was admitted to the Department of Gynaecology and Obstetrics in November 2016 for planned surgical treatment because of uterine myoma. The patient did not report any complaints, and her medical history was irrelevant. Despite excessive menstrual bleedings, the blood picture was in the limits of normal. The routine medical imaging revealed a heterogenous mass, within the anterior uterine wall, approximately 50 mm × 40 mm × 30 mm in size. No non-invasive methods or pharmacological treatment were applied. Due to the deep intramural location of the tumour, a laparotomy was performed. The uterine tumour was removed, and peripheral pelvic

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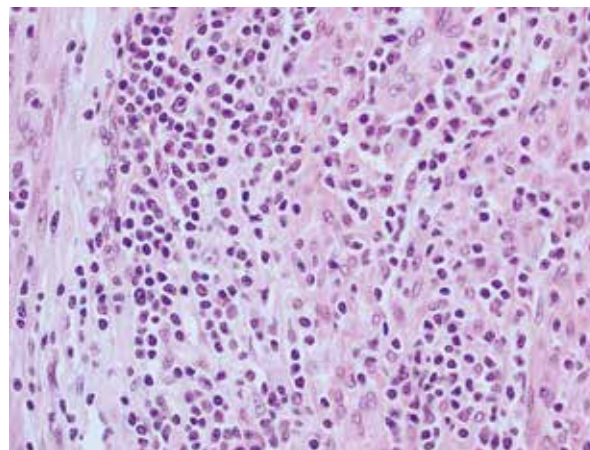
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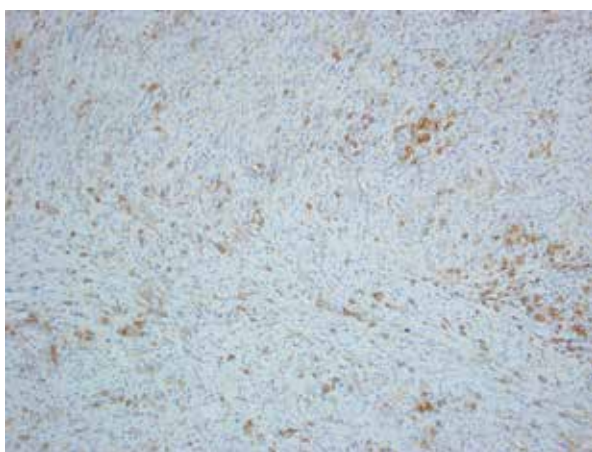
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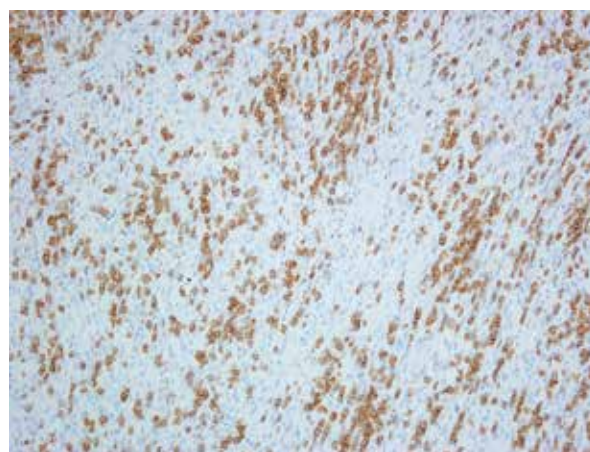
**Fig. 1.** Leiomyoma infiltrated by immune cells, dispersed, and forming nodular aggregate. HE. Obj. magn. 10×



**Fig. 2.** Among the cells infiltrating the leiomyoma – many lymphocytes, scattered few plasma cells and eosinophils. HE. Obj. magn. 60×



**Fig. 3.** Few CD4+ T lymphocytes in the infiltrate of the leiomyoma. CD4 immunostaining. Obj. magn. 20×



**Fig. 4.** CD8+ T lymphocytes prevail in the infiltrate of the leiomyoma. CD8 immunostaining. Obj. magn. 20×

endometriosis (AFS stage I) was coagulated. Both early and distant postoperative courses were uneventful. The patient was discharged from the clinic in good condition on the fifth day after the procedure.

Grossly, the uterine tumour resected measured 7 cm × 4.5 cm × 3.5 cm and had the typical uterine smooth muscle wall consistency.

The microscopic examination revealed the leiomyoma nature of the uterine tumour, accompanied by heavy infiltration composed of mainly T lymphocytes, with moderately high proliferative activity (estimated by Ki67 staining) and aggregates of B lymphocytes, raising suspicion of malignant lymphoproliferation. The material was submitted for consultation to the reference centre in Cracow. The consultation histopathological report confirmed leiomyoma with an unusual picture – infiltrated by lymphocytes, few scattered plasma cells, eosinophils, and mast cells (Figs. 1 and 2). On immunohistochemistry, in the lymphocytic infiltrate the T mature (CD3+/CD5+/TdT–) lymphocytes, small and of cytotoxic (CD8+/CD56–) type, prevailed (Figs. 3 and 4), with moderate prolifera-

tive activity (expression of Ki67 found in ca. 30-40% of the cells), whereas B lymphocytes (CD20+/CD5–/TdT–) were innumerable and present in nodular aggregates. The histopathological diagnosis was established: leiomyoma with massive lymphoid infiltration.

## Discussion

Uterine leiomyomas are the most common neoplasm of the uterus in women. The exact pathogenesis of these tumours remains unknown. An increasing body of evidence suggests that some intrinsic abnormalities of the myometrium, abnormal myometrial receptors for oestrogen, and hormonal changes or altered responses to ischaemic damage during the menstrual period may be responsible for the initiation of (epi)genetic changes in uterine myomas. Transforming growth factor-β3, fibroblast growth factor, epidermal growth factor, and insulin-like growth factor-I are elevated in fibroids. They can contribute to the tumour promotion. Oestrogen and progesterone are also considered to be tumour growth

promoters [3]. Recently, the existence of side population (SP) cells with characteristics of tumour-initiating cells have been characterised in leiomyomas – when exposed to 17 $\beta$ -oestradiol and progesterone, they give rise to fibroid-like tissue *in vivo* [4].

Myomas can be treated in many ways. In minimally invasive procedures, pharmacological treatment, thermoablation, and embolisation of uterine arteries are used. The leading method of treatment is a surgical excision of the tumour, allowing for its histopathological evaluation [5]. Massive lymphocytic infiltration in a myoma is an unusual, rarely seen feature. There are 20 such cases reported in the literature [2]. Some of them, as in our case, raise a strong suspicion of lymphoma, and that neoplasm is mostly considered in differential diagnosis [6].

However, despite the prevalence of lymphocytes in those unusual leiomyomas, the presence of plasma cells, eosinophils, and mastocytes suggest reactive changes. Moreover, the infiltration is limited solely to the removed lesions (not proved in our case). The next rare lesion that has to be included in differential diagnosis is inflammatory pseudotumour of the uterus. Lymphocytes, however, occur occasionally within it, in contrast to the fibroids described, in which lymphocytes are abundant [6]. In the differential diagnosis of leiomyomas with lymphocytic infiltration, the myoma with purulent inflammation (pyomyoma) should also be included. The differential diagnosis between those entities is usually easy.

McClea and McCluggage point out two features that help to identify leiomyoma with lymphoid infiltration. The first one is abundant and extensive infiltration with numerous small mature lymphocytes, and the second one is rich vasculature [7].

More and more frequently, gonadotropin-releasing hormone agonist (GnRH) is used in myoma therapy, to reduce its size. However, sometimes non-invasive techniques do not produce the expected results and require follow-up surgery. Some cases of massive lymphocyte infiltration within the uterine myoma after treatment with GnRH analogues have been reported in the literature [7-9]. It seems that this method predisposes to such a histopathological image of the fibroids.

One of the studies reported the development of such a change in a 59-year-old woman. It has been suggested that lymphocytic infiltration is a post-menopausal process associated with spontaneous uterine fibroid regression [5]. Lymphocytic infiltration may be elicited by a decrease in oestrogen levels or cell death emerging from ischaemia. These processes stimulate an immune response to the degeneration of cellular organelles [10].

## Conclusions

Lymphocytic infiltration within the uterine myoma is rare. The reason for this unusual change is unclear and should be investigated by analysing further cases. The recognition of its distinct histological features is important to avoid possible misdiagnosis of malignant lymphoma, inflammatory pseudotumour, and pyomyoma.

## Disclosure

The authors report no conflict of interest.

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